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Hepatitis B immunity and vaccination coverage among young adult males in the Air Force in South Brazil

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ABSTRACT

We conducted a cross-sectional seroprevalence study to determine hepatitis B vaccination coverage and hepatitis B virus (HBV) immunity in a population of young adult males. Specifically, the population is comprised of Air Force conscripts from the metropolitan region of Florianópolis, Santa Catarina, South Brazil, who were born prior to the full implementation of the HBV vaccination program. Of the 371 young males surveyed, 90% received at least 1 dose of the vaccine and 84% completed the 3-dose schedule. Overall, 57% had positive anti-HBs titers. We must continue to vaccinate individuals up to 20 years of age in order to guarantee a significant reduction in cases of hepatitis B virus.

1. Introduction

Hepatitis B virus (HBV) infection is still a major public health problem in Brazil. It is estimated that at least 15% of the population has been exposed to HBV [1].

Wide territory and cultural and economic differences influence the unequal distribution of hepatitis B throughout the country. Certain areas have a higher HBV prevalence, such as the western Amazon and even some parts of southern Brazil.

Hepatitis B vaccination began in 1989 in some regions of Brazil through immunization campaigns. In 1998, the vaccine became available in more regions to children younger than 1 year of age and to high-risk populations. Afterwards, vaccination coverage was extended to health students, members of the military and adolescents up to 15 years of age. In Santa Catarina, the vaccine was recommended for children younger than 4 in 1993. Then, in 1996, it was recommended for children up to 15 years. It was only in 2001 that the National Immunization Program was extended to all teenagers up to 19 years of age [2].

Recent studies have demonstrated high hepatitis B vaccination coverage among Brazilian children and adolescents, with rates as high as 98% in South Brazil [3–6]. However, current adult vaccination coverage data consists only of estimates based on the number of doses administered among children less than 12 months of age and the estimated cohort.

The achievement of high vaccination coverage in children, adolescents and adults could result in substantial changes in the hepatitis B infection panorama for the near future. Knowing the actual vaccination coverage in adults is important for the evaluation and improvement of current prevention strategies. This study aims to determine the HBV vaccination coverage and HBV immunity in a population of young adult Air Force conscripts in the metropolitan region of Florianópolis (MRF), Santa Catarina, South Brazil.

2. Patients and methods

This cross-sectional seroprevalence study was undertaken to determine vaccination coverage and HBV immunity in young adult males in the MRF, Santa Catarina. The studied population consisted of all conscripts of the Brazilian Air Force at the Air Base of Florianópolis during a 1-year period beginning in June 2009. Military service is mandatory in Brazil, and every male must enroll for service at the selection commission in the year he turns 18, regardless of level of education or socioeconomic status. Each commission is responsible for the conscripts residing in a specific region according to the number of inhabitants of the location.

All conscripts were invited to participate in the study upon their arrival at the Air Force Base. The invitation was extended before any evaluation or test to minimize selection bias.

To successfully estimate vaccination coverage and HBV immunity in this population a minimum sample size of 289 volunteers was calculated to be sufficient at a 95% confidence interval (CI) and 0.05 alpha error (using an expected probability of HBV vaccination of approximately 75%) [7,8].

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Table 1
Socio-demographic characteristics and risk factors of unvaccinated young adult males in the Air Force in South Brazil.

Variable	Unvaccinated		p	Variable	Unvaccinated		p
	n	%			n	%	
Age (years old)				Previous hepatitis			
18	12	7.5	0.035*	Yes	1	25.0	†
19	7	18.9		No	18	9.4	
Ethnicity				Hepatitis in the family			
White	12	8.7	†	Yes	1	4.2	†
Brown/Black	7	12.1		No	18	10.5	
Marital status				Blood transfusion			
In a relationship	4	12.1	†	Yes	1	25.0	†
No relationship	15	9.2		No	18	9.4	
Education				Piercings or tattoos			
<High school	11	16.9	0.016*	Yes	6	11.3	†
≥High school	8	6.1		No	13	9.1	
Parents education				IDU			
≤High school	15	8.9	†	Yes	0	0.0	†
>High school	4	14.8		No	19	9.7	
Residency				Unsafe sex			
Florianópolis	15	11.5	†	Yes	8	10.1	†
MRF	4	6.2		No	11	9.4	
Occupation				MSM			
Yes	9	9.1	†	Yes	1	100.0	†
No	10	10.3		No	18	9.2	
HMI				STD			
1–4	12	9.4	†	Yes	0	0.0	†
5 or more	7	10.1		No	19	9.7	

n, number of unvaccinated subjects; MRF, metropolitan region of Florianópolis; HMI, household monthly income (minimum wages); IDU, intravenous drug use; MSM, men who have sex with men; STD, sexually transmitted diseases.

* Significant at $p < 0.05$ in chi-squared test.

† $p > 0.2$ in chi-squared test.

Approval for the study was obtained from the Ethics Committee of the Federal University of Santa Catarina (protocol 136/2009), and written informed consent was obtained from all study participants.

A self-administered standard questionnaire, adapted from one previously established and tested [9], was provided to each subject. The questionnaire asked for socio-demographic characteristics including age, ethnicity, marital status, highest level of education achieved by the subject and his parents, residency, occupation and household monthly income. In addition, the questionnaire asked about HBV-related risk factors such as a personal or family history of hepatitis, blood transfusions, tattoos or piercings, intravenous drug use, unsafe sex, having sex with another man, and history of sexually transmitted diseases.

Vaccination cards (VCs) were checked in order to assess coverage characteristics including vaccination status, number of doses received, and age at the time of vaccination.

Blood samples were obtained from all enrolled subjects and stored at −20 °C during transportation to the Laboratory of Clinical Analysis at the Federal University of Santa Catarina Hospital. HBsAg, anti-HBc, anti-HBs and anti-HCV serologies were obtained, and each test was performed using automated microparticles enzymatic immunoassay (Abbott®, AxSYM System, Wiesbaden, Germany). HBsAg, anti-HBc and anti-HCV results were categorized as either "positive" or "negative" according to the provided cut-offs. Anti-HBs titers were categorized as "undetectable" if anti-HBs was less than the cut-off value, "detectable" if anti-HBs was less than 10 mIU/mL, and "reactive" if anti-HBs was greater than or equal to 10 mIU/mL, according to the manufacturer's instructions.

Positive cases were referred to the nearest health care center for confirmatory tests and to receive further counseling and monitoring. None of the participants tested positive for HBsAg or anti-HCV. Four subjects were anti-HBc positive and anti-HBs reactive, and two subjects were only anti-HBc positive.

Bivariate analysis included Pearson's chi-square test for the comparison of categorical values using a significance level of $p < 0.050$. Non-conditional logistic regression was used in univariate and multivariate analysis to identify associations between dependent and independent variables. This model included variables significant at $p < 0.200$ in Pearson's chi-square test. All reported values were two-tailed. The dependent variables included "non-vaccination", "non-reactive anti-HBs (<10 mIU/mL)", "vaccinated by the age of 6–18 years", and "receiving only 1 or 2 doses of the HBV vaccine (incomplete vaccination schedule)". The independent variables are listed in Tables 1–4. Results are presented as odds ratios and include the respective 95% CIs.

All data were entered into and analyzed using SPSS version 11.0 (SPSS Inc., Chicago, IL, USA).

3. Results

A total of 410 young males were invited to enter the study, and 371 agreed to participate (91% acceptance). The remaining 39 refused to participate. Among those that entered the study, 53% (196) had VCs.

Vaccination coverage was 90% among subjects with VCs. When subjects without VCs were considered unvaccinated, the vaccination rate of the total sample dropped to 50%.

In all, 84% of subjects with VCs completed the 3-dose schedule. Among this group, vaccination occurred during the first 5 years of life in 57% of subjects.

Table 1 presents socio-demographic characteristics as well as possible risk factors for HBV infection among unvaccinated subjects. These unvaccinated adults were older and less educated than those who were vaccinated (Table 2).

Of all the adults studied, 41% had reactive anti-HBs titers, 16% had detectable antibodies, and 43% had undetectable anti-HBs. Non-reactive anti-HBs titers (<10 mIU/mL) were present in 46% of vaccinated subjects and in all of the unvaccinated participants. A non-reactive anti-HBs titer was significantly associated with non-vaccination ($p < 0.0001$; OR 22.28; 95% CI 2.92–170.12), vaccine receipt between birth and 5 years of age, and receiving only 1 or 2 doses of the HBV vaccine (Table 3).

Table 2
Univariate and multivariate logistic regression analysis of the association between non-vaccination and significant variables ($p < 0.2$ in chi-square test).

Variable	Unvaccinated (% (*n*/*N*))	*p*	OR (95% CI)	
			Univariate	Multivariate
Age (years old)				
18	7.5 (12/159)	0.035*	1	1
19	18.9 (7/37)		2.86 (1.04–7.86)*	2.77 (0.99–7.76)
Education				
<High school	16.9 (11/65)	0.016*	3.13 (1.19–8.22)*	3.06 (1.15–8.12)*
≥High school	6.1 (8/131)		1	1

n/*N*, ratio between unvaccinated subjects and total number of individuals in the row; OR, odds ratio; CI, confidence interval.
* Significant at $p < 0.05$.

Table 3
Univariate and multivariate logistic regression analysis of the association between non-reactive anti-HBs (<10 mIU/mL) and significant vaccine coverage characteristics ($p < 0.2$ in chi-square test).

Variable	Non-reactive anti-HBs < 10 mIU/mL (% (*n*/*N*))	*p*	OR (95% CI)	
			Univariate	Multivariate
Age at vaccination				
0–5 years old	57.4 (58/101)	<0.001*	3.11 (1.66–5.83)*	4.91 (2.35–10.23)*
6–18 years old	30.3 (23/76)		1	1
Vaccine doses				
1–2 doses	64.3 (18/28)	0.032*	2.46 (1.06–5.68)*	5.23 (1.97–13.88)*
3 doses	42.3 (63/149)		1	1

n/*N*, ratio between subjects with non-reactive anti-HBs and total number of individuals in the row; OR, odds ratio; CI, confidence interval.
* Significant at $p < 0.05$.

Older adults were more likely to have been vaccinated between the ages of 6 and 18 years and were more likely to have unsafe sexual risk factor (Table 4A). Receiving only 1 or 2 doses of the HBV vaccine was associated with having piercings or tattoos (Table 4B). Those men who received the HBV vaccine between the ages of 6 and 18 were more likely to have an incomplete vaccination schedule ($p < 0.001$; OR 5.13; 95% CI 2.05–12.84).

Young men without a VC were more likely to be less educated, to be employed, to have less educated parents, and to have a lower household income (data not shown). In addition, adults

Table 4
Univariate and multivariate logistic regression analysis of the association between vaccination by the age of 6–18 years (A), receiving 1–2 doses of the HBV vaccine (B) and significant variables ($p < 0.2$ in chi-square test).

	Vaccination by the age of 6–18 years (% (*n*/*N*))	*p*	OR (95% CI)	
			Univariate	Multivariate
(A)				
Age (years old)				
18	37.4 (55/147)	0.001*	1	1
19	70.0 (21/30)		3.90 (1.67–9.13)*	3.81 (1.60–9.06)*
Parents education				
≤High school	44.8 (69/154)	0.194	1.86 (0.72–4.77)	2.04 (0.76–5.50)
>High school	30.4 (7/23)		1	1
Unsafe sex				
Yes	53.5 (38/71)	0.020*	2.06 (1.12–3.80)*	2.00 (1.06–3.78)*
No	35.8 (38/106)		1	1
	Receiving 1–2 doses of the HBV vaccine (% (*n*/*N*))	*p*	OR (95% CI)	
			Univariate	Multivariate
(B)				
Age (years old)				
18	13.6 (20/147)	0.074	1	1
19	26.7 (8/30)		2.31 (0.91–5.90)	2.19 (0.84–5.70)
Piercings or tattoos				
Yes	25.5 (12/47)	0.033*	2.44 (1.06–5.65)*	2.20 (0.92–5.23)
No	12.3 (16/130)		1	1
Unsafe sex				
Yes	21.1 (15/71)	0.113	1.92 (0.85–4.32)	1.57 (0.68–3.66)
No	12.3 (13/106)		1	1

n/*N*, ratio between subjects (A) vaccinated by the age from 6 to 18 years (B) who received 1–2 doses of the HBV vaccine and total number of individuals in the row; OR, odds ratio; CI, confidence interval.
* Significant at $p < 0.05$.

without VCs were more likely to have undetectable anti-HBs titers ($p < 0.0001$; OR 2.51; 95% CI 1.64–3.82).

Overall, 70% of the studied adults had been vaccinated and/or had positive anti-HBs titers.

4. Discussion

Since the hepatitis B vaccine was included in the Brazilian National Immunization Program, there has been a substantial increase in vaccination coverage, especially among children and adolescents [3]. However, cases of hepatitis B have not appeared to decrease accordingly, probably due to long incubation and latency periods, the misdiagnosis of acute cases, and underreporting of disease [10]. Mandatory screening has reduced the transmission of HBV through blood transfusions, but sexual transmission remains a concern among unvaccinated adolescents and adults. This raises questions regarding the need to promote vaccination through educational campaigns, whether the vaccination strategy has been adequate, and whether vaccination coverage is high enough to decrease the occurrence of disease [3].

This vaccination coverage analysis showed a lower rate of vaccination than the current estimates, which suggest that 75% of the population younger than 20 years old in Brazil has been vaccinated [10]. Considering the vaccination coverage of subjects in this study and the anti-HBs detectable titers, the actual vaccination coverage in this population may vary between 57 and 70%. Nevertheless, this coverage is quite low considering that the current hepatitis B vaccination strategy should guarantee the vaccination of all individuals up to age 20.

Approximately 2/3 of all individuals with proven vaccination history received the last dose of the vaccine during the first five years of life. Higher dropout rates among subjects vaccinated at older ages reinforce the importance of vaccinating children after birth, the best way of guaranteeing completion of the 3-dose schedule. Additionally, other vaccines have high coverage, so there should be an improvement in coverage if the hepatitis B vaccine is administered at the same visit as other routine immunizations.

The association between low levels of education and non-vaccination highlights the importance of reaching lower income families with vaccination awareness campaigns. That is, education and socioeconomic status are often linked.

Likewise, a central database should connect each individual to a vaccination card. This card should be required upon admission to school.

Positive anti-HBs serology implies HBV immunity, which may be acquired through HBV infection or vaccination. Primary vaccination with a 3-dose series results in seroprotection (defined as the development of anti-HBs levels $\geq$10 mIU/mL) in at least 95% of vaccinated individuals. However, following completion of the primary series, anti-HBs titers decline and may fall below this threshold, sometimes to undetectable levels. Recent studies argue that immunologic memory persists and would be capable of preventing chronic or symptomatic infections for up to 22 years after vaccination [11–15]. The rates of HBV immunity in this study may be between 57 and 70% as the result of the intersection between subjects who were vaccinated and those with detectable anti-HBs. The assumption that the rate of anti-HBs decreases through the years is reinforced by the observation that, in this study, adults receiving the HBV vaccine at younger ages (0–5 years) were more likely to have non-reactive anti-HBs titers.

The importance of completing the 3-dose series of the HBV vaccine is further highlighted by the association between receiving only 1–2 doses of the HBV vaccine and having a non-reactive anti-HBs titer (<10 mIU/mL). However, it is unclear in this case whether the non-reactive anti-HBs are associated with a lack of seroprotection following incomplete vaccination or are expected as antibodies decrease.

The observation that subjects without VCs were more likely to have undetectable anti-HBs titers may be a result of non-vaccination. However, this might also reflect the younger age at vaccination for this group and a subsequent decrease in anti-HBs, a possibility that should not be ruled out.

Associations between unsafe sex, piercings or tattoos and vaccine coverage characteristics (such as vaccination by the age of 6–18 years and receiving 1–2 doses of the HBV vaccine) also demonstrate the importance of educational campaigns as fundamental tools for the horizontal transmission of hepatitis B. Unsafe sex and obtaining piercings or tattoos without precautionary steps may represent potential sources of percutaneous exposure [16,17]. The results of this study are concerning, as these risk factors were more common in individuals who received only one or two doses of the HBV vaccine and/or remained unvaccinated at the age of 6–18 years.

This study demonstrated, for the first time, the rates of HBV immunity and vaccination coverage in young adults in the MRF using documented data and serological analysis. This study shows that there is still an urgent need to improve hepatitis B vaccination in this region. The substantial rate of unvaccinated young adults here suggests that vaccine coverage among adults older than 19 may be even more concerning. Therefore, we must continue our efforts to vaccinate individuals younger than 20. In addition, prevention and awareness campaigns must be improved. These campaigns should promote safe sex and reach all people. Furthermore, the creation of vaccination campaigns targeted at adults should be evaluated, in order to decrease the rate of HBV infections. With a decrease in rates of HBV, public health resources could potentially be redirected from treating HBV to treating other diseases that cannot be so easily prevented.

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